DSSTox Field Definition File:

EPA Fathead Minnow Acute Toxicity Database (EPAFHM)

(last updated 10 April 2006)

Description: Information in this file is intended to provide a minimum level of annotation to the DSSTox SDF file created for the EPA Fathead Minnow Acute Toxicity Database (EPAFHM) obtained from the Source website. For further explanation of Source-specific fields, a user is encouraged to consult the listed references. Additional information is provided on the DSSTox EPAFHM SDF Download Page http://www.epa.gov/nheerl/dsstox/sdf_epafhm.html. A number of modifications in fields (and allowable contents) were made to the original EPA Fathead Minnow database to improve consistency in notations, eliminate the need for table addendums, and facilitate use of the DSSTox SDF files in relational searching applications. All modifications are documented in the ***Comments*** section of the table below. In the course of creating the DSSTox SDF files, it was noted that the Source EPA Fathead Minnow database included a single LC50 test result rather than a geometric mean when multiple (2-10) bioassays were performed on a single chemical. Replicate bioassays were conducted on 98 chemicals in the database. In order to align with the Main Citation - Appendix 2, these replicate experiments are not listed separately in the DSSTox EPAFHM SDF file; rather a single geometric mean of replicate LC50 values for each of the 98 chemicals is reported. As a result of this finding, specific listings of all 137 replicate LC50 experiments for the 98 chemicals were added to the original Source EPA Fathead Minnow database.

Previously, all ***DSSTox Standard Chemical Field*** definitions were provided in the NAMEID_FieldDefFile. Since all DSSTox Structure Data Files contain the same full complement of ***DSSTox Standard Chemical Fields*** (with a few of these fields optional), users are now referred to NAMEID SDF Download Page and the central reference documentation file located at:
http://www.epa.gov/nheerl/dsstox//DSSToxAboutDSSTox/MoreonStandardChemFields/StandardChemFieldDefTable_08Dec2005.doc

The first section of the Table below lists the ***DSSTox Standard Toxicity Fields*** employed for this database, followed by the ***EPAFHM Source-Specific Fields*** containing the toxicity information particular to EPAFHM. The ***DSSTox SDF*** column lists SDF files in which the corresponding ***Field Name*** is present. All ***Units*** and ***Descriptions*** are extracted from Source reference materials unless otherwise noted. ***Allowable Values*** list allowed field entries occurring in CPDBAS, separated by slashes for exclusive entries (i.e., cannot occur with another entry) and commas or spaces for non-exclusive entries (i.e., can occur with other values). These are defined and explained in the ***Description*** section; italicized note refers to the type of entry (e.g., *Text*); the pound symbol (#) indicates that the ***Allowable Values*** entry is a number.

Source Website: http://www.epa.gov/med/databases/fathead_minnow.htm

Source Contact: Scientific questions pertaining to the EPAFHM database should be directed to Chris Russom, Mid-continent Ecology Division, National Health & Environmental Effects Research Laboratory, US EPA, Duluth, MN; email: russom.chris@epa.gov

Main Citation: Publications reporting use of the DSSTox SDF file for the EPA Fathead Minnow database are asked to list the full DSSTox file name, including date stamp, and to cite as primary reference the following:

> Russom, C.L., S.P. Bradbury, S.J. Broderius, D.E. Hammermeister, and R.A. Drummond (1997) Predicting modes of action from chemical structure: Acute toxicity in the fathead minnow (*Pimephales promelas*). *Environmental Toxicology and Chemistry* 16(5): 948-967. *
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> **pdf of Main Citation can be downloaded from EPAFHM SDF Download Page at the central DSSTox website:*
> http://www.epa.gov/nheerl/dsstox/sdf_epafhm.html

SDF Usage Notes:
Each DSSTox SDF file contains a single **STRUCTURE** field. For each chemical record, the **STRUCTURE** field entry directly corresponds to the content of the **STRUCTURE_...** fields. The **STRUCTURE_Shown** field documents the relationship between what is displayed in the **STRUCTURE** field and the actual tested chemical substance, i.e. **TestSubstance_...** fields, with the latter corresponding directly to the toxicity data field entries. Commercial chemical relational database (CRD) applications may automatically insert one or more structure identifier fields upon import or export of an SDF file (e.g., Formula, FW or Mol_ID), fields that

may augment or duplicate one or more of the DSSTox Standard Chemical Fields. Since the proper ordering of fields upon SDF import into most applications requires a non-blank entry in each field of the first database record, the word "blank" is inserted in each empty text field in Record 1 for this purpose; this word should be deleted from Record 1 fields after SDF import by the user is complete, particularly in the case of pure numeric fields. Users are additionally cautioned that some fields (**STRUCTURE_SMILES** and **STRUCTURE_InChI**, in particular) may exceed the 200 character limit specified in the MDL CTFiles SDF standard (see http://www.epa.gov/nheerl/dsstox/MoreonSDFs.html), and that some CRD applications may insert a line break or truncate these fields upon SDF import or export. Finally, CRD application-specific molecular header information in the SDF file is deleted in the final DSSTox SDF files; users using CRD applications requiring a molecule header upon import of the SDF can specify either **DSSTox_SID** or **DSSTox_ID_FileName**. Upon SDF import, **DSSTox_CID** can be used to identify and manage chemical structure duplicates.

As an MS Word document, the following table is best viewed onscreen using either Normal or Web Layout View in Landscape page orientation.

Field Name	***DSSTox SDF***	***Units***	***Allowable Values***	***Description***	***Comments***
			DSSTox Standard Toxicity Fields		
Study Type *(no spaces)*	All		acute toxicity	Field is used to label all records in the database, generally with the same entry, and is designed to facilitate record identification for cross-database structure searching. Field entry refers to the main type of toxicity study for which data is represented in the database.	Field names and content are being coordinated with the public ToxML standardization effort.
Endpoint	All		LC50	Field is used to label all records in the database, generally with the same entry, and is designed to facilitate record identification for cross-database structure searching. Field entry refers to the type of toxicity measure represented within the database.	Field names and content are being coordinated with the public ToxML standardization effort.
Species	All where applicable		fathead minnow	Field is used to label all records in the database, generally with the same entry, and is designed to facilitate record identification for cross-database structure searching. Field entry refers to the species of animal(s) listed in the data record and used in the toxicity study or studies.	Field names and content are being coordinated with the public ToxML standardization effort.
			EPAFHM Source-Specific Fields		
ChemClass_FHM	EPAFHM	*None*	Alkanes/ Alkenes/ Saturated Hydrocarbons/ Unsaturated Hydrocarbons/ Basic Ethers/ Diphenyl Ethers/ Cyclic Ethers/ Basic Alcohols/ Alkene Alcohols/ Alkyne Alcohols/ Diols/ Aldehydes/ Basic Ketones/ beta Diketones/ Cyclic Ketones/ Carboxylic Acids/	Standard organic chemical class designations of the sort used in traditional QSAR studies. These class designations are only provided for information purposes in EPAFHM and were not used in the construction of Mode-of-action (MOA) classes or derivation of quantitative structure-activity relationships (QSARs) for this study.	To facilitate use of EPA Fathead Minnow database in a relational format, we have replaced the original field "CODE" with new field "ChemClass FHM", which contains the organic chemical class referenced in the "CODE" field and listed in a Table 2 addendum in the original EPA Fathead Minnow database. DSSTox field entries exactly correspond to original EPA Fathead Minnow database CODE Table 2 entries with the exception that commas are deleted from Primary, Secondary, Tertiary, aliphatic and aromatic amines class names, and hyphens are deleted from 5-membered ring aliphatics

			Basic Esters/ Phthalates/ Amides/ Acrylates/ Nitriles/ Primary aliphatic amines/ Secondary aliphatic amines/ Tertiary aliphatic amines/ Primary aromatic amines/		and aromatics, beta-Diketones, hetero-atom compounds, and DEAS-complex structures class names. DEAS stands for “Drug Enforcement Agency Structures”, a broad functional categorization.

CLOGP	EPAFHM	*None*	#	Logarithm of the octanol:water partition coefficient (LogP) computed using the semiempirical fragment-based method applied in the CLOGP software [2], unless M appears in MLOGP field in which case the measured LogP value is provided in the **CLOGP** field from the STARLIST database of CLOGP.	
MLOGP	EPAFHM	*None*	M/	If "M" entry, the CLOGP field value is obtained from the STARLIST database of experimentally measured LogP values provided in the CLOGP application [2]. If *blank* entry, the CLOGP field value is computed from the CLOGP semiempirical fragment-based method.	
LC50_mg	EPAFHM	mg/l	#	96 h LC50 (concentration producing lethality in 50% of test animals after 96 hours exposure) in mg/l. Calculated using Spearman-Karber method [3]. Geometric mean of LC50s presented if more than one bioassay conducted for the chemical. If no mortality, or less than 50% mortality observed at 96 h, LC50 field left *blank*.	If insufficient mortality was observed, LC50 was assigned a value of -99 in the original EPA Fathead Minnow database. To avoid problems when log(LC50) is used in QSAR, we convert these to *blank* entry in LC50 field. Replicate experiments used to compute geometric mean LC50 values for 98 chemicals are listed in revised EPA Fathead Minnow database located at Source website. Geometric mean LC50 value for pentachlorophenol is reported in DSSTox SDF. Replaces **LC50** field name.
LC50_mmol	EPAFHM	mmol/l	#	Conversion of **LC50_mg** to mmol units: **LC50_mmol** = **LC50_mg** / **STRUCTURE_MolecularWeight**	Field new to v3a.
LC50_Note	EPAFHM	*None*	*Text*	Comments regarding the LC50 result, pertaining to exceptional situations, e.g., where: 50% mortality could not be achieved at saturation concentrations, non-monitonical pattern of death was observed (i.e., more deaths at lower concentrations than at higher concentrations), or exceptions were made in terms of pH or mixtures. If more than one replicate bioassay, number of experiments contributing to calculation of the geometric mean LC50 is specified.	Replaces REMARKS field in original EPA Fathead Minnow database; eliminate use of abbreviations for mortality and saturation. When more than one bioassay was performed on chemical, note refers to single test result. A note was added to the DSSTox SDF specifying the number of experiments (2-10) contributing to calculation of the geometric mean LC50. Replaces **LC50NOTE** field name.
LC50_Ratio	EPAFHM	*None*	# r48 r72 NM/ NR/ NT/ ND/	Used for dose-response assessments in the estimation of MOA; entry is ratio of 24 h LC50/96 h LC50. For exposures where a 24 h LC50 was not available, these codes follow the ratio: r48 = 48h/96h ratio r72 = 72h/96h ratio NM = non-monitonical pattern of death (i.e. more deaths at lower concentrations than at higher concentrations) NR = LC50 obtained only at 96 h, so no ratio is possible NT = indicates chemical was not toxic in 96 h exposure	Text codes (r48, r72, NR) were substituted for the following symbol codes used in the original EPA Fathead Minnow database: * = 48h/96h ratio = r48 # = 72h/96h ratio = r72 ** = LC50 obtained at 96 h = NR NM, NT not defined in original EPAFHM documentation In case of replicate experiments, ratio for a single replicate is reported that approximately represents group.

				ND = value not determined	Replaces **LC50RATIO** field name.

MOA	EPAFHM	*None*	NARCOSIS I/ NARCOSIS II/ NARCOSIS III/ NARCOSIS I and II/ UNCOUPLER/ ACHE/ BLOCKER/ REACTIVE/ NEUROTOX/ NEURODEP/ UNSURE/ MIXED/ ND/	Mode-of-action of chemical assigned by authors of study based on joint toxic action studies, establishment of toxicodynamic profiles, and behavioral and dose-response interpretation of 96 h (hour) LC50 tests. MOA field entries are defined below, with further explanation provided in Recommended Citation listed above (Russom et al., 1997): NARCOSIS I = Base-line narcosis, or Narcosis I NARCOSIS II = Polar narcosis, or Narcosis II NARCOSIS III = Narcosis III primarily observed in esters and some acrylates NARCOSIS I and II = Identified as both Narcosis I & II UNCOUPLER = Uncoupler of oxidative phosphorylation ACHE = Acetylcholinesterase inhibition BLOCKER = Respiratory blocker/inhibitor REACTIVE = Electrophile/proelectrophile reactivity NEUROTOX = Central nervous system seizure/stimulant NEURODEP = Neurodepressant UNSURE = MOA could not be determined - insufficient evidence MIXED = MOA could not be determined - conflicting evidence ND = MOA was not determined either because the chemical was not toxic at saturation or the test result was obtained after the MOA analysis was conducted.	Field content provided in Table 3 addendum to original EPA Fathead Minnow database, referenced to MOA_NUM codes. The latter field and codes, used by the authors for a specific application, were deemed unnecessary for inclusion in the DSSTox SDF. Original **MOA** field entries in the EPA Fathead Minnow database (e.g., REACTIVE_1, _2, _3, _4) corresponding to a single MOA with different levels of confidence (A,B,C,D) have been collapsed into a single MOA field for the DSSTox SDF (e.g., REACTIVE). The level of confidence is specified in a newly added field, **MOA_Confidence**. In addition, some common MOA categories that were listed separately for chemical classes were combined into the single MOA category and symbols in MOA names were eliminated: NARC_ACRYLATE = NARCOSIS III NARCO_ESTER = NARCOSIS III NARC_AMINE = NARCOSIS II NARCOSIS_I&II = NARCOSIS I and II EMPTY = ND
MOA_Confidence	EPAFHM	*None*	A/ B/ C/ D/	Level of confidence placed in **MOA** classification based on available evidence, ranging from A (highest) to D (lowest): A = FATS, joint toxicity determination and/or chemical-specific literature confirmation B = behavior syndrome, LC50_Ratio, and TOXINDEX value all consistent with structurally similar chemical with MOA assignment and A level confidence; also if LC50 ratio and TOXINDEX consistent with prototypical compound in MOA group C = less than 3 level B components, but additional supporting information available (s.a. concentration/response slope, behavior comments, chemical similarity to prototypical compound) D = no confidence in MOA classification due to insufficient data *blank* = no MOA assigned hence no level of confidence listed	New field added to DSSTox SDF to accommodate information that had previously been combined into MOA field in original EPA Fathead Minnow database, e.g.: MOA=REACTIVE_1 converts to MOA=REACTIVE, MOA_Confidence =A MOA=REACTIVE_2 converts to MOA=REACTIVE, MOA_Confidence=B etc. Replaces **MOACONF** field name.
MOA_Mixture Test ***(no spaces)***	EPAFHM	*None*	NARCOSIS I/ NARCOSIS II/ NARCOSIS I and II/ UNCOUPLER/ BLOCKER/	If a mixture test was conducted and the chemical was additive with a chemical of known **MOA** as described by Broderius et al. [4], an **MOA** was assigned (see MOA field definitions). *blank* entry indicates no mixture test was performed.	Replaces MIXINDEX field in original EPA Fathead Minnow database, with numerical index entry replaced by the corresponding **MOA** text as follows: 0= *blank* (no mixture test) 1= NARCOSIS I 2 = NARCOSIS II

					12 = NARCOSIS I and II 3= UNCOUPLER 4= BLOCKER Replaces **MIXMOA** field name.
ExcessToxicity Index ***(no spaces)***	EPAFHM	*None*	#	Ratio of the predicted toxicity of the compound using Narcosis I QSAR equation of Veith et al. [5], Log molar LC50 = -0.94 log*P* + log(0.000068**P* +1) – 1.25 (*P*=octanol/water partition coeff), divided by the actual LC50, used as a measure of excess toxicity. TOXINDEX values greater than 10 are considered indicative of compounds not acting by Narcosis I mode of action. Contributes to determination of level of confidence of MOA assignment.	Replaces **TOXINDEX** field name.
FishAcuteTox Syndrome ***(no spaces)***	EPAFHM	*None*	NARCOSIS I/ NARCOSIS II/ UNCOUPLER/ BLOCKER/ REACTIVE/ ACHE/	If a fish acute toxicity syndrome (FATS) test was conducted using rainbow trout as described by McKim et al. [6,7], the MOA that was determined from that test is listed. FATS MOA assignments consistent with MOA assignment of chemical from other indicators for fathead minnow provide the highest level of confidence (A) to the chemical MOA assignment (see MOA field definitions). *blank* entry indicates no FATS test was performed.	MOA codes used in the original EPA Fathead Minnow database field have been replaced with the corresponding MOA name in DSSTox SDF: N-1 = NARCOSIS I N-2 = NARCOSIS II UNC = UNCOUPLER RBK = (Respiratory) BLOCKER IRR = (Irritants) REACTIVE ACH = ACHE Replaces **FATS** field name.
FishBehaviorTest ***(no spaces)***	EPAFHM	*None*	TYPE I/ TYPE II/ TYPE III/ TYPE III/ CONFLICT/ EL, ID, PHPROB/	Behavior signs of stress were identified for fathead minnows exposed to toxicants and were used to classify chemicals into three behavioral syndromes as described by Drummond and Russom [8]. These were used to determine level of confidence of MOA assignment. TYPE I = depressed locomotor activity with little or no response to outside stimuli, darkened body color, most fish dead by 24 h TYPE II = hyperactive, usually overreactive to outside stimuli, death typically within several days of exposure TYPE III = spontaneous locomotor activity, high incidence of convulsion, spasms, tetany, scoliosis, lordosis, and/or hemorrhaging in vertebral column CONFLICT = conflicting information EL = refers to tests conducted in electronic diluter systems ID = insufficient data PHPROB = indicates pH problem with study *blank* entry means no checklist was done for bioassay	Hyphens used in original database have been eliminated, e.g., TYPE I-ID converts to TYPE I ID Replaces **BEHAVIOR** field name.

Additional EPAFHM references:

1. Anderson, E., G.D. Veith, and D. Weininger (1987) SMILES: A line notation and computerized interpreter for chemical structure. EPA/600/M-87-021. Technical Report. U.S. Environmental Protection Agency, Environmental Research Laboratory, Duluth, MN, USA.

2. CLOGP™ program version 3.4 and STARLIST database, respectively, within the UDRIVE system version 3.53, 1988, from Pomona College Medicinal Chemistry Project, Claremont, CA.

3. Hamilton, M.A., R.C. Russo, and R.V. Thurston (1977) Trimmed Spearman-Karber method for estimating median lethal concentrations in toxicity bioassays. *Environ. Sci. & Technol.* 11: 714-719. Correction 12: 417.

4. Broderius, S., M. Kahl, and M. Hoglund (1995) Use of Joint Toxic Response to define the primary mode of toxic action for diverse industrial organic chemicals. *Environ Toxicol Chem* 14: 1591-1605.

5. Veith, G. D., D.J. Call, and L.T. Brooke (1983) Structure-toxicity relationships for the fathead minnow, *Pimephales promelas*: narcotic industrial chemicals. *Can. J. Fish. Aquat. Sci.* 40: 743-748.

6. McKim, J.M., P.K. Schmieder, R.W. Carlson, E.P. Hunt, and G.J. Niemi (1987) Use of respiratory-cardiovascular responses of rainbow trout (*Salmo gairdneri*) in identifying Fish Acute Toxicity Syndromes. Part I. Pentachlorophenol, 2,4-dinitrophenol, tricaine methanesulfonate, and 1-octanol. *Environ. Toxicol. Chem.* 6: 295-312.

7. McKim, J.M., P.K. Schmieder, G.J. Niemi, R.W. Carlson, and T.R. Henry (1987) Use of respiratory-cardiovascular responses of rainbow trout (*Salmo gairdneri*) in identifying Fish Acute Toxicity Syndromes. Part II. Malathion, carbaryl, acrolein, and benzaldehyde. *Environ. Toxicol. Chem.* 6: 313-328.

8. Drummond, R.A. and C.L. Russom (1990) Behavioral toxicity syndromes: A promising tool for assessing toxicity mechanisms in juvenile fathead minnows. *Environ. Toxicol. Chem.* 9: 37-46.